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10/575,261	04/10/2006	Kenya Shitara	Q105979	9631

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EXAMINER	
DAHLE, CHUN WU	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
02/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/575,261	SHITARA ET AL.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,13 and 16-39* is/are pending in the application.

4a) Of the above claim(s) *13,17-19,21-35,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,16, 20,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to the claims, filed on November 17, 2009, is acknowledged.

Claims 7-12, 14, and 15 have been canceled.
Claims 1-6, 13, and 16-39 are pending.

Claims 13, 17-19, 21-35, 38, and 39 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 3, 2009.

Claims 1-6, 16, 20, 36, and 37 are currently under consideration as being read on the elected invention of a fusion protein of a soluble TNF receptor II.

2. This Office Action will be in response to applicant's arguments, filed on November 17, 2009.

The rejections of record can be found in the previous Office Action, mailed on August 17, 2009.

3. The Examiner acknowledges that this application claims foreign priority to JAPAN 2003-350158 and that a certified copy of the priority document has been received.

4. Applicant's amendment to the specification, filed on November 17, 2009, is entered.

5. In view of applicant's amendment to the claims, the prior objection to claim 20 has been withdrawn.

6. In view of applicant's amendment to the claims, the prior rejection under 35 U.S.C. 112, second paragraph, against claim 16 has been withdrawn.

7. In view of applicant's assurance regarding the deposit of the Biological Material produced by cell deposited as FERM BP-8499 (see pages 12-13 of the Remarks and Statement of Availability filed on November 17, 2009), the prior rejection under 35 U.S.C. 112, first paragraph, enablement, against claim 16 has been withdrawn.

8. Claim 16 is objected to following informality:

Claim 16 is drawn to the fusion protein produced by FERM BP-8499. Applicant is suggested to amend the claims to recite "a cell deposited as FERM BP-8499" for clarity.

9. This is a **New Ground of Rejection** necessitated by applicant's amendment to the claims. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is indefinite because it is depended upon canceled claim 14. For examination purposes, claim 16 is read as a dependent claim of claim 1.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-6, 20, 36, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kanda et al. (US 2003/0115614, reference of record) for reasons of record.

The previous Office Action (mailed on August 17, 2009) states:

"*Kanda et al. teach an antibody or a fusion protein composition and a medicament thereof comprising an antibody with an Fc region wherein the Fc region comprises complex type N-glycoside-linked sugar chains having a structure in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chain (e.g. see paragraphs [0240], [0258] and claims 41 and 54-56). Kanda et al. further teach said Fc region can be of human IgG1 subclass comprising a hinge region, a CH2 and a CH3 region (e.g. see paragraphs [0245]-[0258]). Furthermore, Kanda et al. teach said fusion protein can be a dimer (e.g. see paragraph [0257]). Moreover, Kanda et al. teach that said fusion protein exhibits enhanced effector function including antibody-dependent cell mediated cytotoxicity (ADCC) (e.g. see paragraphs [0262]-[0264]). In addition, Kanda et al. teach that said fusion protein or antibody can be produced by a host cells that are transformed with DNA encoding the fusion protein or antibody following with purifying the protein or antibody from the culture medium (e.g. see claims 1-20).*"

Applicant's arguments, submitted on November 17, 2009, have been fully considered but have not been found persuasive.

Applicant asserts that independent claim 1 has been amended to limit the recited soluble receptor to soluble TNF comprising SEQ ID NO:64 which is not taught by Kanda et al. Thus, applicant argues that the rejection should be withdrawn.

This is not found persuasive for following reasons:

In contrast to applicant's assertion, it is noted that the amendment to the independent claim 1 only limited the scope of the soluble receptor recited in the Markush

language to be SEQ ID NO:64 but does not narrow the other components recited in the Markush language including a single chain antibody, or any ligand protein. Therefore, the instant claims are read as a fusion protein composition comprising a fusion protein of a binding protein wherein the binding protein comprises at least one protein selected from the group consisting of a single chain antibody, a soluble receptor of TNF comprising SEQ ID NO:64 and a ligand protein wherein the fusion protein comprises an antibody Fc region with the recited N-glycoside sugar chain structure.

Given that Kanda et al. teach the binding protein being antibody including single chain antibody (e.g. see paragraph [0253] of Kanda et al.) with N-glycan structure with fucose not bound to N-acetylglucosamine in the reducing end in the sugar chain, the referenced antibody composition meet the claimed limitation.

Therefore, applicant's arguments have not been found persuasive.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-6, 20, 36, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Presta (US 2003/0157108, reference of record) in view of Jacobs et al. (US Patent 5,605,690, reference of record) for reasons of record.

The previous Office Action (mailed on August 17, 2009) states:

"Presta teaches immunoadhesin, e.g. soluble TNFR combined with IgG Fc region, can be used as therapeutics to treat human diseases by blocking ligand receptor interaction and recruit the immune system effector cells to kill target cells (e.g. see paragraphs [0008]-[0009] and [0352]-[0374]). Presta further teaches glycoproteins including immunoadhesins comprising Fc region wherein the Fc region comprises complex sugar structure that lacks fucose (e.g. see SUMMARY OF THE INVENTION on pages 4-5). Thus, the prior art's glycoproteins comprises Fc region with N-glycoside linked sugar in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chains. Furthermore, Presta teaches that said glycoproteins comprising said N-linked sugar structures exhibits superior affinity to FcγRIII (F158) and enhanced ADCC effect than glycoproteins with fucose (e.g. see paragraph [0042])/

The reference teachings differ from the claimed invention by not describing soluble TNFR II comprising SEQ ID NO:64.

Jacobs et al. teach dimerized soluble TNF receptor conjugated with human IgG1 Fc region (e.g. see Figures 1 and 2 and claim 1). The prior art soluble TNF receptor is 100% identical in amino acid sequence to the instant SEQ ID NO:64 recited in claim 15 (see sequence alignment attached to this Office Action)."

Applicant's arguments, filed on November 17, 2009, have been fully considered but have not been found persuasive.

Applicant argues that Presta does not teach an antibody composition comprising 100% of antibodies without fucose attached to the N-glycan. Applicant relies upon examples disclosed in Figure 1B and Table I and asserts that Presta only teach antibody composition produced by CHO lec13 cells with reduced (not eliminated) GDP-mannose 4,6-dehydratase (GMD) activity. Thus, applicant argues that the Presta does not produce a composition of antibodies wherein 100% of the antibodies are fucose-free. Further, applicant argues that Presta does not teach soluble TNF receptor comprising SEQ ID NO:64. Thus, applicant argues that the rejection should be withdrawn.

This is not found persuasive for following reasons:

Contrary to applicant's reliance on specific examples of the prior art, it is noted that a prior art reference must be considered in its entirety, see MPEP 2141.02. In this case, Presta's teachings are not limited to the working examples of antibody composition produced using CHO lec13. Presta recognizes that host cell with reduced enzyme (e.g. GMD) would produce antibody composition with reduced fucose content and teach that following strategies can be used to achieve antibody composition containing 100% antibody or fusion protein without fucose: (a) using engineered host cell unable to express fucosylate protein and obtaining from transformaant with DNA encoding the fusion protein or antibody and purifying from the culture (b) adjusting culturing conditions preventing fucosylation, (c) post-translational removal of fucose, (d) selecting only antibody without fucose attached to the N-glycan by using lectin columns (e.g. see paragraphs [0178]-[0196]). Further, Presta claims a composition comprising glycoprotein (e.g. antibody) comprising an Fc region wherein 100% of the glycoprotein lacking fucose and methods of producing such composition (e.g. see claims 1-41). Therefore, Presta teaches glycoprotein composition comprising soluble TNFR combined with IgG Fc region. Further, Presta teaches that the Fc region can be from human IgG1 with CH2 and CH3 domain (e.g. see claims 1-41).

Moreover, in response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combination of references. See MPEP 2145.

It is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Furthermore, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

Here, as stated previously, it would thus be obvious to one of skill in the art at the time of the invention to combine the teachings of Presta with Jacobs et al. to make soluble TNFRII-Fc protein with N-glycan sugar structures in which fucose is not bound to N-acetylglucosamine because al the claimed elements were known in the prior art and one of skilled artisan could have combined the elements by known methods taught by Presta with no change in their respective functions, and the combination would have yielded predictable results. Further, a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention for enhanced ADCC effect of the soluble TNFRII-Fc and there would have been a reasonable expectation of success.

Therefore, applicant's arguments have not been found persuasive.

15. Conclusion: no claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ram Shukla can be reached 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Dahle
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